

REMARKS

The present application is directed to biocompatible, polymerizable macromer compositions that release or produce nitric oxide (NO) under physiological conditions. The compositions are applied to sites on or in a patient in need of treatment for disorders such as restenosis, thrombosis, asthma, wound healing, penile erectile dysfunction or the like, or can be applied to the surface of a medical device, such as a stent, for example. After the macromer composition is polymerized, the nitric oxide or nitric oxide modulating compounds are released *in situ* to elevate or otherwise modulate nitric oxide levels at the site where treatment is desired.

The term “macromer” is known to those skilled in the art as a macromolecular monomer or “prepolymer”. A feature of the macromer is that it retains the ability to be further polymerized. Polymerization of the macromer results in the formation of a polymer. Applicants note that, for the sake of clarity, the term “macromer” is specifically defined in the claims as being “polymerizable”.

Support for the amendment to Claim 1 is found at page 4, lines 9-12.

Rejection Under 35 U.S.C. § 112, second paragraph

The Office Action rejects Claim 2 under 35 U.S.C. § 112, second paragraph, as indefinite because it is not clear how a macromer can comprise additional macromers.

Applicants respectfully submit that Claim 1 is directed to a “macromer composition” wherein at least one of the elements is a macromer, and another element is a NO carrying region or NO modulating compound. In Claim 1, the macromer is further described as comprising regions. Claim 1 has been amended to more clearly define the invention. Applicant submits that in Claim 2, additional macromers are claimed as being part of the “macromer composition”.

Therefore, Applicants respectfully submit that Claim 2 is no longer indefinite and request that the rejection be withdrawn in light of the amendment to Claim 1.

Rejection Under 35 U.S.C. § 103

The Office Action rejects Claims 1-23 under 35 U.S.C. § 103, as being unpatentable over Ragheb *et al.* or Keefer *et al.* in view of Hubbell *et al.* or Igo *et al.* in view of Hubbell *et al.*

The Office Action states that Ragheb provides a medical device comprising a porous layer composed of a polymer, which controls the delivery of a bioactive agent.

The Office Action further states that the polymers of Ragheb are derived from polymerizable monomers.

Applicants respectfully submit that Ragheb does not teach the delivery of a bioactive agent bound to a **polymerizable macromer** as claimed in the present application. Ragheb teaches a bioactive agent bound to a porous polymer such as polyamide, parylene or a parylene derivative. None of these polymers are **polymerizable**. Release of the agent in Ragheb is through the porous polymer, not polymerization of a macromer. Applicant further submits that, generally, all polymers are derived from polymerizable subunits.

The Office Action states that Keefer discloses a method of releasing NO with a NO-releasing agent, wherein the NO-releasing agent can be a polymer.

Applicants respectfully submit that Keefer does not teach a nitric oxide-releasing agent bound to a **polymerizable macromer** as claimed in the present application. Keefer teaches a nitric oxide-releasing agent bound to a polymer such as poly(lactide/glycolide), polyethyleneimine, aminopolystyrene, polyethyleneglycol, or a mixture thereof. None of these polymers are **polymerizable**.

The Office Action states that Igo administers NO through a biodegradable polymer.

Applicants respectfully submit that Igo does not teach a nitric oxide-releasing agent bound to a **polymerizable macromer** as claimed in the present application. Igo teaches a nitric oxide-releasing agent bound to a **biodegradable polymer** for the release of NO. Claim 1 of the present invention, on the other hand, recites "wherein NO or NO modulating compound is released from the macromer composition following polymerization".

The Office Action states that Hubbel provides multifunctional polymers for use in inhibiting cell adhesion, said polymers including biocompatible polymers, such as PVP and PVA. The Examiner further states that Hubbel teaches that polymers exhibiting more than one manner of degradation are required in some cases.

Applicants submit, however, that Hubbel does not teach the delivery of a bioactive agent bound to a **polymerizable macromer** as claimed in the present application. Hubbel teaches a bioactive agent bound to a **biodegradable polymer** for the release of NO. Claim 1 of the present invention, on the other hand, recites "wherein NO or NO modulating compound is released from the macromer composition following polymerization".

Therefore, it is seen that none of the references teach the composition of the present invention, which releases or produces nitric oxide (NO) upon polymerization of the macromers of the macromer composition. Additionally, as the Office Action noted several times, none of the references specify the various regions of the monomers in the polymer. Therefore, Applicants respectfully submit that it could not have been obvious to one having ordinary skill in the art at the time the invention was made, to apply or modify any of the teachings of the cited references, to prepare the composition as claimed in the present invention.

Version with Markings to Show Changes Made

Amendments in the Claims:

In accordance with 37 CFR 1.121(c), the following versions of the claims as rewritten by the foregoing amendment show all the changes made relative to the previous versions of the claims.

1. A biocompatible, polymerizable, macromer composition comprising a macromer bound to at least one NO carrying region or NO modulating compound, wherein NO or NO modulating compound is released from the macromer composition following polymerization, under physiological conditions, wherein the macromers comprise regions selected from the group consisting of water soluble regions, tissue adhesive regions, and polymerizable end group regions.

CONCLUSION

The foregoing is submitted as a full and complete Response to the Office Action mailed November 6, 2001. Enclosed herewith is a Petition for a One-Month Extension of Time and \$55 check to cover the fee for a small entity. No additional fees are believed due; however, the Commissioner is hereby authorized to charge any additional fees which may be required, or credit any overpayment to Deposit Account No. 11-0855.

Applicants submit that this Response places the pending claims in the present application in condition for allowance, and such action is courteously solicited. The Examiner is invited and encouraged to contact the undersigned attorney of record if such contact will facilitate an efficient examination and allowance of the application (404-745-2413).

Respectfully submitted,
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